DEPARTMENT OF HEALTH & HUMAN SERVICES

Substance Abuse and Mental Health Services Administration

Center for Mental Health Services
Center for Substance Abuse Prevention
Center for Substance Abuse Treatment
Rockville MD 20857

JUL 18 2003

Dear Colleague:

Opioid Treatment Programs (OTPs), States, and patients have made numerous inquiries to the Substance Abuse and Mental Health Services Administration's (SAMHSA) Center for Substance Abuse Treatment (CSAT) regarding the adequacy of oral fluid testing in OTPs. Therefore, CSAT is generating additional guidance on the adequacy of oral fluid testing in OTPs as a part of its role under Title 42 of the Code of Federal Regulations (CFR) § 8.12(f)(6). This regulation requires opioid treatment programs (OTPs) to provide adequate testing or analysis for drugs of abuse, including at least eight random drug abuse tests per year per patient in maintenance treatment, in accordance with generally accepted clinical practice.

CSAT has initiated the development of two relevant Treatment Improvement Protocols (TIPs). One will address opioid agonist treatment, including the issue of drug testing in OTPs. The other will address drug testing more generally including medical, office-based treatment. These TIPs are intended to provide guidance to OTPs and other substance abuse treatment providers on the use of testing procedures for addiction treatment, including alternative testing such as oral fluid testing. Release of the TIPs is expected early in 2004.

CSAT requested that its National Advisory Council review the use of this emerging technology and consider the need for interim guidance to the field. On September 20, 2002, the CSAT National Advisory Council established a Subcommittee on Oral Fluid Testing chaired by Louis Baxter, M.D. The Subcommittee reviewed several recent scientific articles on the subject of oral fluid testing together with direct information provided by experts in toxicological testing and opioid addiction treatment. Subsequently, on March 12, 2003, the CSAT National Advisory Council endorsed the Subcommittee's report and recommendations.

The enclosed Report of the CSAT National Advisory Council Subcommittee on Oral Fluid Testing represents the Center's interim guidance on the use of oral fluid testing in OTPs, until more detailed guidance in subsequent TIPs is available. Importantly, the guidance provides that off-site drug testing using oral fluids may be adequate, at least in some populations, for the purposes of 42 CFR § 8.12(f)(6). It is CSAT's view that there is now sufficient information available for medical directors to make a determination of the adequacy of oral fluid testing in the opioid treatment program setting.

This letter reflects guidance and elaboration on the SAMHSA/CSAT opioid treatment regulations. However, it is also important for OTPs to conform to appropriate State laws and regulations in this area.

If you have further questions about this policy or oral fluid testing in OTPs, please contact Alan Trachtenberg, M.D., M.P.H., Division of Pharmacologic Therapies, SAMHSA/CSAT, telephone (301) 443-7745.

Sincerely,

H. Westley Clark, M.D., J.D., M.P.H., CAS, FASAM
Director
Center for Substance Abuse Treatment

Enclosure

Report of the CSAT National Advisory Council (NAC) Subcommittee on Oral Fluid Testing

(3/11/2003)

Louis Baxter, MD, Chair;
Alan Trachtenberg, MD, MPH, Exec. Sec.

The subcommittee held its first meeting on Wednesday morning, November 20, 2002, in the 10th floor Conference room of the Rockwall II Building in North Bethesda, MD.
Members present were Louis Baxter, Richard Suchinsky and Pamela Jumper Thurman (by phone). Outside consultants in attendance consisted of Ira Marion (Albert Einstein Medical College, NYC) , Mark Parrino (AATOD), Ron Jackson (Evergreen Treatment Services, Seattle, WA) and Edward Cone (formerly of NIDA's Intramural Research Program). Federal staff present included Donna Bush and Bob Stephenson (CSAP); Todd Rosendale, Nick Reuter, Arlene Stanton, Bob Lubran, and Alan Trachtenberg (CSAT).

The meeting was extremely informative and the distributed materials were of great value, especially Dr. Edward Cone's article, from the July, 2002 issue of the *Journal of Analytic Toxicology* and an article by Eric Wish and George Yacoubian on "A Comparison of Saliva Testing to Urinalysis in an Arrestee Population", which had appeared in the September, 2001 issue of the *Journal of Psychoactive Drugs*. An important presentation was offered by Dr. Cone, with data that were published (J Anal Toxicol 2002 Nov-Dec;26(8):541-6) soon after the meeting.

Urinalysis Testing as the "Gold Standard"

RTI International and the Walsh Group prepared a brief paper comparing oral fluid (OF) with other drug testing matrices. This paper was also used as a resource for a consensus panel that met the following two days, also chaired by Dr. Baxter, which is drafting comprehensive guidelines for the use of drug testing in clinical addiction treatment (under a CSAT task order with RTI). The RTI report notes that "Because drug excretion in urine is well understood and urinalysis drug testing methodology is well established, urinalysis has become the standard to which other technologies are compared." The report goes on to cite another important finding. "Oral fluid testing is occurring in the United States and at least two laboratories are testing large numbers of oral fluid samples. Additionally, both point of care (POC) testing and lab based testing are currently practiced in an unregulated market. There is currently only one POC test on the market that has U.S. Food and Drug Administration (FDA) approval, and this test is only a two-panel test for methadone and opiates."

Finally, the RTI/Walsh report indicates that "the testing industry has pursued and developed POC oral fluid tests which are currently on the market. There are, however, concerns about the quality of these tests."

The Yacoubian article cites an interesting reference, which is pertinent to this point of discussion. "While urinalysis is generally recognized as the reference standard, a method recently introduced in non-laboratory settings for ascertaining drug use - saliva testing - may offer an alternative to urinalysis".

The Need for More Comprehensive Studies - Comparing Urine Testing with OF Testing

The Yacoubian and Cone articles agreed on the need for additional study. Yacoubian makes the following statement. "The authors concluded that a more comprehensive study to evaluate the efficacy of saliva testing in field research is warranted." Dr. Cone provides an informative overview in his abstract to the article. "Draft guidelines for the use of oral fluid for workplace drug testing are under development by SAMHSA in cooperation with industry and researchers. Comparison studies about the effectiveness of oral fluid testing versus urine testing are needed to establish scientifically reliable cut-off concentrations for oral fluid testing."

An interesting point of discussion emerged during the meeting of November 20, 2002 and it was found that drug testing issues that are important to workplace testing differ from the issues that are of importance to analyzing drug testing results in drug treatment programs. While there are serious consequences in both environments, the OTP environment, as an illustration, would be utilizing the results of drug tests, either urinalysis or OF, to make decisions about take-home medication, dose adjustment and/or the need for more intensive treatment.

In view of the fact that the SAMHSA/CSAT OTP accreditation regulations require only a minimum of eight drug tests per year, it is critical to have a scientifically-based and clinically effective test, which will guide clinicians in the OTPs to make the most informed clinical decisions. It is also understood that analyzing drug testing information within the OTP is but one factor in making such clinical decisions. It is, however, a critical component of the clinical decision making process in opioid agonist treatment for opiate addiction, conducted under 42CFR part 8, regulated by SAMHSA.

The Benefits of Utilizing OF Testing in a Program Environment

It is clear that OF testing offers certain benefits in OTPs. Dr. Cone's article cites the obvious point. "Specimens can be readily collected under observed conditions without invasion of privacy, thus precluding substitution or deliberate adulteration." It is clear that most patients would prefer OF testing in view of the numerous comments/complaints that have been made about how OTPs throughout the country adopt various, relatively more or less objectionable methods of observing and collecting urine samples. The OF testing mechanism is simpler and affords the individual patient far greater dignity. However, while POC testing of urine, right there and then in the treatment program, is technologically feasible and clinically desirable, POC testing of OF is not yet technically dependable and would not be considered adequate under 42CFR8. So the remainder of this report specifically supports only the collection of OF sample in the clinic, with shipping of the sample and analysis taking place in a CLIA-certified clinical laboratory.

Critical Points of Concern

The Yacoubian article makes an important point, which should be critical for the use of OF testing in substance abuse treatment programs, given the importance that clinicians place on drug testing results in making clinical decisions about take-home medication and dose adjustments. "While the detection time for urinalysis is up to 72 hours for most illegal drugs of abuse, saliva tests have a shorter detection period of only 12 - 24 hours. Saliva tests may, therefore, offer the advantage of being able to detect only very recent drug use. This may be important for detecting impairment near the time of an accident or crime, or for testing employees with high-risk occupations." This makes the point of how tests will be employed in different environments, workplace versus drug treatment programs.

In view of the fact that 42CFR8 requires only 8 drug tests per annum within OTPs and given the fact that the regulations allow programs to dispense up to 30 take-home doses to patients at the conclusion of a two-year period of stability, the integrity and quality of the drug testing modality is quite important. What may be an advantage to the workplace may be a disadvantage to the OTP in this context.

In spite of this, there appears to be value in OF testing. The Yacoubian article makes the point. "It was also found that urinalysis and saliva testing detected almost identical rates of cocaine and heroin use. These findings suggest that saliva testing may be as accurate a tool as urinalysis for detecting recent cocaine and heroin use among criminal populations, but may be inappropriate for detecting recent marijuana use." As you will note, there is no discussion of methadone and OF testing in the aforementioned articles. However, further search has revealed yet unpublished data from Wish & Yacoubian specifically addressing patients in outpatient addiction treatment, including patients on Methadone. Without any specific funding, Wish & Yacoubian collected urine and OF specimens from 163 adult intensive outpatient and methadone maintenance treatment clients in Baltimore. With laboratory urinalysis as the reference standard, the Intercept Oral Specimen Collection Device (IOSCD)® was 100% sensitive and 100% specific for benzodiazepines, 82% sensitive and 96% specific for cocaine, 100% sensitive and 92% specific for methadone, and 83% sensitive and 99% specific for opiates. For marijuana, the sensitivity was 39% and the specificity was 93%. These authors were unable to utilize definitive GCMS testing to resolve discrepant pairs of OF and urine from the same patient/time. Therefore, this study, by itself, is unable to determine which test matrix is absolutely the most accurate. Issues raised to potentially explain discrepant results include the longer period of the "detection window" for urine testing and the availability of various means of falsifying urine specimens, making urine potentially less sensitive in comparison to oral fluid specimens which may currently be harder to falsify.

Recommendations

The following excerpts from the aforementioned articles and comments lead to a greater support for conducting comparison parallel field tests of OF testing to urine testing in OTPs throughout the country.

There were a number of observations that emerged from the November 20, 2002 meeting:

- It is clear that OTPs and state regulatory authorities need guidance from SAMHSA/CSAT on the use of OF testing as an approved testing device in meeting the federally driven accreditation criteria.

  Illustratively, two states have competing perspectives. The State Methadone Authority in Texas issued a written memorandum to all the methadone programs within its jurisdiction, indicating that OF testing cannot be used at the present time. Accordingly, programs that were using OF testing are prohibited from doing so. The state of Rhode Island has forwarded correspondence to CSAT, indicating that programs within its jurisdiction would like to use OF testing. The state supported this request and is still waiting for a response from CSAT.

- Different OTPs throughout the United States are struggling with the decision to use OF testing in addition to or instead of urine testing as the standard of detection in making important clinical decisions. Some programs have evidently switched over already to the use of OF testing for all of their patients. Other programs have been comparing OF testing result findings with urine test findings. Some programs are gradually introducing OF testing as an alternative, on an as-needed basis.

- There was also a discussion of using OTPs as a living laboratory, making organized clinical comparisons between OF and urinalysis testing instruments. While the market can be involved in supporting such comparisons (i.e. laboratory testing companies), it still needs to be organized, utilizing consistently applied methods. There could be a great benefit to coordinating the work of OTPs, government agencies and testing product manufacturers in executing this "living laboratory".

In conclusion, the meeting of November 20, 2002 was an important step. Off-site drug testing of OF may be adequate, at least in some populations, for the purposes of 42CFR8. Point of Care (onsite) testing of oral fluids does not appear adequate for these purposes. Properly conducted POC urine testing, on the other hand, is adequate and probably offers clinical benefits, in terms of rapidity of clinically feedback, over and above those of laboratory testing of either OF or urine. All of these, and even hair testing, may be of utility in selected patients. Over time, it is hoped that clinics will adopt a flexible and medically oriented approach that makes cost effective use of

the available technology. Drug testing is a medical service and therefore decisions about how it should be done, or when/whether it can be changed, are completely within the purview of the program's Medical Director. In making a decision to implement new non-standard test protocols, the Medical Director would be well advised to fully inform himself or herself about the specifics of both the new test matrix and the specific laboratory's methods, and to make reasonable efforts to assure and document the adequacy of the new test in the population served by the clinic. Marketers of new, nonstandard testing modalities should be encouraged to support an adequate period of duplicate/parallel testing to help their customers make the most responsible medical decisions about the replacement of standard testing with new technologies. Discordant results from immunologic testing of the two matrices being compared should preferably be adjudicated by confirmatory GCMS testing down to the limits of detection (LOD) or Limits of Quantitation (LOQ) for the lab doing the testing, to make the best assessment of comparative sensitivity and specificity. The recommendation for a run-in period of parallel testing is one that would help both the individual clinic and the field as a whole, but cannot be considered mandatory. It should also be remembered that the regulatorily specified minimum annual number of tests is truly a minimum, and that for many patients, adequate medical care will really require significantly more testing than this minimum standard. It is also absolutely vital that testing be truly random, and that patients remain "at risk" for a second test in any given month, and that occasionally, to be truly random, a second test may follow a first test by less than a week. Additional tests should also be performed when clinically indicated by the appearance of intoxication. POC testing (of urine) may be especially helpful for this purpose.

Over time, we may expect to see the evolution of more complex testing protocols that offer clinicians and their patients a choice; or combinations of POC urine testing, lab-based OF testing and perhaps even hair testing (for instance, in patients with 30 day take homes), based on a clinical indications, and individual patient, physician and program preferences.

It would be the subcommittee's recommendation for this report to be presented to the next meeting of CSAT's National Advisory Council, along with a presentation from Wish & Yacoubian of their new parallel testing data from methadone treatment populations. If approved by the council, this report can then be disseminated to the field, in support of the Program Medical Directors, who will be making the final choices as to their OTP's testing protocols. Leaving this important medical decision to local medical judgement will be an important example of CSAT's overall regulatory approach to opioid agonist therapy, which is that this is a medical treatment for a chronic illness, in which medical decisions are best left in medical hands.